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A New Biochemical Test For Pregnancy

The author has developed a biochemical pregnancy test of high dependability, simple to perform, and requiring a minimum of time, equipment and expense, of approximately 100 percent accuracy for both pregnant and nonpregnant subjects. The test requires only 2 special test tubes and 4 reagents. The technic is so simple that the physician, nurse or technician can perform the test in 30 minutes or less. The diagnostic reaction is a distinctly brown color which can be read with the naked eye, without mechanical aid. Animals are totally unnecessary for the test.

The product of pregnancy, which is identified by this test, is free estrone. Although estrone is found in the normal nonpregnant individual, it is not present in a sufficient quantity to cause a positive response, since the essential reagent used is calibrated to such strength that it does not produce a positive reaction with the lesser amount of free estrone present in the nonpregnant individual. There are 2 pathological conditions, however, which produce a positive reaction: hydatidiform mole and chorionepithelioma. As with the biological tests, the response in these conditions is quite significant and they are positive with very high dilutions of urine. The simplicity of the test is also of advantage in diagnosing complete recovery from these conditions as indicated by negative reactions.

Mechanism of Test. The test depends upon the presence of a substantial amount of free estrone in the urine of pregnant women. Since female urine contains progesterone in substantial amounts at certain menstrual phases, for purposes of identifying a pregnancy test it is necessary that the estrone and progesterone be separated, thus assuring that progesterone is absent from the solution to be tested for the reaction with the color-producing reagent.

This separation of estrone from progesterone and other possible interfering substances in the urine is accomplished by use of the fact that steroid salts, such as sodium salts, are insoluble in chloroform, while the nonsalt form of steroids is, as a rule, soluble. The steroids which might reasonably be expected to be present in the urine are soluble in chloroform. Since estrone, the hormone which is to be identified, contains a phenolic hydroxyl group, it is sufficiently acid to react with sodium hydroxide to form sodium estronate. This salt is not soluble in chloroform; hence, if a solution containing this salt is extracted with chloroform, the sodium estronate will remain in the aqueous solution, while the chloroform-soluble substances are extracted from it.

The mechanical separation of the layer of chloroform and alkalinized urine is made simple by special extracting tubes. The outer chamber is a screw cap test tube with 2 cc. and 5 cc. calibration, the first to measure the urine and the second the chloroform. The second, or inner tube, is a regular test tube with a round hole perforated at a level so as to be safely above the 5 cc. mark. This second tube must be just enough smaller than the first so that it may be inserted into the first tube to enable the estrone extractive to rise around it and to flow through the hole of the second or inner tube. The material drawn off in this manner is the extractive and contains the free estrone to be identified.

The solution of estrone is then caused to couple chemically either with 2, 4-dinitrophenyldiazine in an acid medium which is then alkalinized for color formation, or with meta-dinitrobenzene in an alkaline solution. In the first instance, a stable brown color indicates the presence of estrone, while, in the second instance, the development of a red color is the positive sign. The brown color formed by the coupling of 2,4-dinitrophenylhydrazine with estrone is that of the sodium salt of 2,4-dinitrophenylhydrazone of estrone, while the red color produced with the meta-dinitrobenzene and estrone represents not a chemical coupling, but rather a color complex between the two.

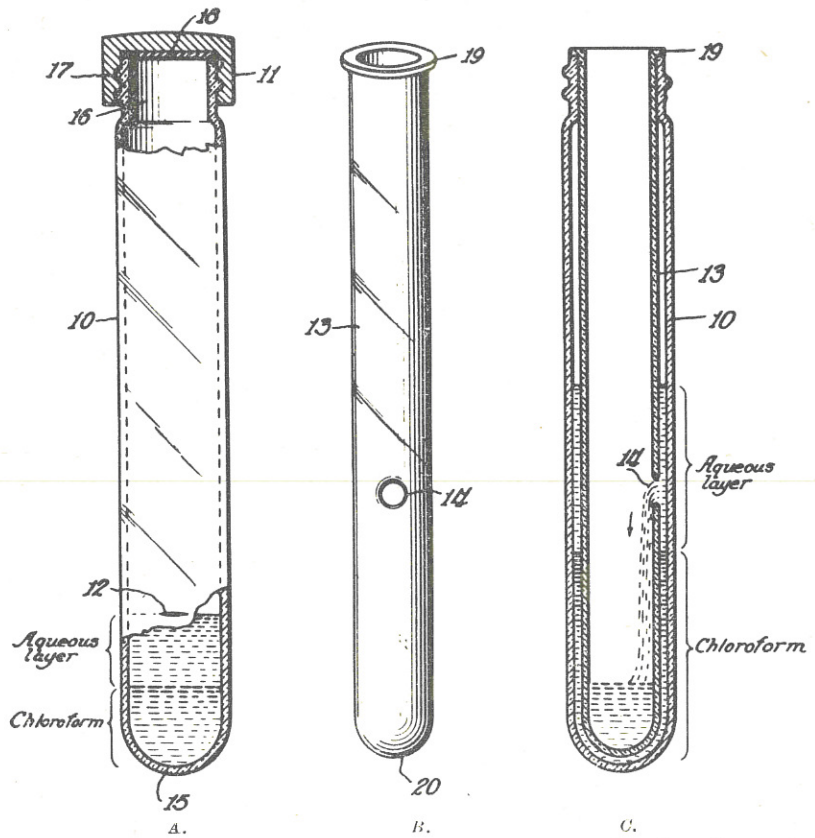

Fig. 1.—*A*, Shows the outer tube, with the aqueous and chloroform layers in place. *B*, Shows the inner tube. Item 14 is the hole through which the aqueous layer flows when the two tubes are put together. *C*, Shows the two tubes together. Note that the aqueous layer, being the upper stratum, flows through the hole, while the chloroform layer remains in the outer tube.

Technical Procedure. The directions for performing the biochemical test for pregnancy are as follows:

Procedure A.-

1. Place 2 ml. of urine in the outer chamber or tube of the extraction apparatus.
2. Add 2 drops of Reagent I (0.5 normal sodium hydroxide) and mix well.
3. Add Reagent II (chloroform, U. S. P.) up to the second mark on the extraction chamber.
4. Close the chamber with the screw cap and shake vigorously for at least 30 seconds.

5. Allow to stand quietly until the two layers have separated sharply (about 1 minute).

6. Remove the screw cap and insert the inner tube of the extraction apparatus slowly into the outer chamber until the tube is completely inserted. Care should be exercised not to mix the layers, as only the upper, clear stratum is desired for testing.

7. Separate the two tubes and discard the solution in the outer chamber. Rinse this with water and pour contents of inner tube into the outer extraction chamber.

8. Add 4 drops of Reagent III (0.5 normal sulfuric acid) and mix well.

9. Add 5 drops of Reagent IV (saturated 2,4-dinitrophenylhydrazine in 70 percent ethanol). This solution must not be more than 24 hours old. Mix well and allow to stand 10 to 15 minutes to permit complete coupling of reagent with free estrone.

10. Add 2 cc. of Reagent I, mix well, and observe.

11. The presence of a brown color which persists for 2 minutes or more is positive for pregnancy. Fading of the brown color to the usual clear amber urine color or to a colorless state is negative and free estrone is not present. Procedure B.- Proceed as in Procedure A, through Steps 1, 2, 3, 4, 5, 6 and 7.

8. Add 5 drops of Reagent V (freshly prepared 1 percent metadinitrobenzene in ethanol).

9. Add 1 ml. of Reagent VI (15 percent potassium hydroxide) and mix.

10. Allow to stand about 10 minutes.

11. Observe colors. If there is a reddish-violet color, the test is positive; if not reddish-violet, the test is negative for pregnancy.

Procedures A and B are two separate tests for pregnancy. If it is desired to have a check on Procedure A, both tests may be run at the same time by doubling the amount of the reagents up to and including Step 7. Thereafter the end steps must be included for completion only, as it was known that metadinitrobenzene would produce a color reaction with estrone. This latter procedure, however, is subject to failure due to certain drug reactions and should not be depended upon unless the patient is advised to avoid all medications whatsoever for 48 hours before collecting the urine to be tested.

Comment. The present series consisted of 1,640 individual cases on which tests were performed at various months of pregnancy in order to determine the over-all accuracy and also to ascertain if there were any variable factors from month to month which would affect the accuracy; 2,560 tests were performed. In this series, 2,537 were positive, with an accuracy of 99.1 percent. There were 23 negative reactions, giving an error of 0.9 percent. In addition to the 1,640 pregnancies, 500 known or alleged nonpregnant individuals were tested without error. In this series, toxemia did not sufficiently lower the free estrone content of the urine to be detrimental to the test. Hypertensive patients were classified as having pre-eclampsia or threatened eclampsia, with or without albuminuria and essential hypertension. Fifty-nine patients showed albuminuria, 53 were free of albuminuria and there were 5 cases of essential hypertension.

In these 117 cases, all tests were positive. In 2, the fetal heart tones were absent. Two patients were syphilitic with negative Kahn tests following treatment. Two with positive pregnancy tests had glycosuria with albuminuria and 1 without. Two patients showed positive pregnancy tests and were pregnant but had negative Friedman tests. Only 1 patient had a negative test after previously having been positive.

In 2 cases of hydatidiform mole the test was positive with high dilutions of urine and in 2 cases of chorionepithelioma the same was true. All 4 became negative within 10 weeks following treatment, indicating complete recovery, thus offering a good prognosis. Thus it is seen that this test may aid in the final prognosis as well as diagnosis.

Table I is a tabulation of the 1,640 cases with 2,560 tests by months of gestation.

TABLE I.

MONTH	CASES	POSITIVE	NEGATIVE
First	218	206	12
Second	574	572	2
Third	308	304	4
Fourth	181	180	1
Fifth	204	202	2
Sixth	183	183	0
Seventh	216	215	1
Eighth	291	290	1
Ninth	385	385	0
Total	2,560	2,537	23
Per cent	100	99.1	0.9

The return of the test to negative following delivery is naturally dependent upon complete removal of all placental tissue, which required but a few days. Only 4 patients were positive at the time of their final examinations at 6 weeks. In the threatened abortion cases tested, 4 were positive, and abortion was incomplete while 9 were negative, and dilatation and curettage failed to produce any living chorionic tissue. It would seem, therefore, that a negative test would indicate complete abortion, complete placental separation, or placental death and interference would be indicated only by hemorrhage. Four of 5 tubal pregnancies were positive. The reaction is positive with blood serum as well as with urine. Urine, as for other tests, should be filtered or centrifuged; blood requires centrifuging. Uterine fibroids do not produce a positive test.

How early pregnancy can be diagnosed is a moot question, as the patient presents herself for care only after the first missed period. In this series, however, there were 3 patients who had been undergoing sterility study. During this time they presented weekly specimens in anticipation of becoming pregnant and met with success. In these 3 cases, positive tests were obtained before the first missed period.

The possible causes for failure of the test present few minor difficulties that might confuse the issue. Brief consideration, however, is warranted. Ketosis from diabetes or starvation would present a different reaction, to say nothing of their individual diagnostic characteristics. Phenylpyruvic acid in the urine produces reactions unlikely to be confused. Pyruvic acid is unlikely to be present in the urine; its color curve is different and the cause may be readily determined.

For laboratory and hospital purposes, photoelectric colorimetric methods are adaptable for quantitative determination which would be of value in both direct and differential diagnosis. (Am. J. Obst. & Gynec., June '51, G. C. Richardson)

Procaine Amide for Prophylaxis and Therapy of Cardiac Arrhythmias Occurring During Thoracic Surgery

Cardiac arrhythmias occurring during general anesthesia occur frequently and are more readily detected by the electrocardiogram than by palpation. They may be classified as to rate, origin of pacemaker and whether paroxysmal or sustained. From studies of artifically induced arrhythmias in experimental animals, the observation has been made that rhythmic abnormalities ordinarily considered to be of minor importance may be potentially dangerous during surgery and general anesthesia. This is especially true of ventricular rhythms. The occurrence of ventricular premature contractions, isolated or coupled, is regarded as relatively innocuous, whereas ventricular tachycardia, which may evolve into ventricular fibrillation, is regarded as serious.

Procaine, diethylaminoethanol, dibenamine and quinidine are among the drugs which have been employed for therapy of ventricular arrhythmias. Intravenous procaine has been the most widely used during anesthesia and has provided the best results. The amide of procaine, hereinafter referred to as pronestyl, has been recently developed as a drug which may be safely administered in relatively large doses and which will exert the desired effects of procaine for prolonged periods. It is not hydrolyzed by the enzyme which affects procaine, and hence is relatively stable in vivo. Gastrointestinal absorption is rapid and complete. Administered intravenously in therapeutic dosage to conscious subjects, pronestyl does not stimulate the central nervous system as does procaine. Hypotension occurs only occasionally following intravenous administration of the drug, and this is both moderate and transient. Studies in conscious cardiac patients have demonstrated the efficacy of this drug in treatment of ventricular arrhythmias.

Prophylaxis. In this study of patients undergoing thoracic surgery during cyclopropane anesthesia pronestyl, administered prophylactically, reduced the incidence of all types of arrhythmias, and especially of ventricular arrhythmias, for extended periods of time. Ventricular arrhythmias in the control series occupied 8.1 percent of the total anesthesia time; in the experimental series, 3.2 percent. The difference in incidence of arrhythmias in the 2 series of patients was marked despite the presence of several factors which would tend to minimize any differences between them. Patients in the control series were younger; only 10 underwent intrathoracic operations; the average duration of anesthesia was considerably less than in the experimental series; and these patients were generally healthier than those in the experimental series, the difference in health being chiefly a difference in pulmonary function and reserve.

Ventricular tachycardia, which is considered to be a serious ventricular arrhythmia, was infrequently encountered in this study, but much more often in

the control series (11 times, in 6 patients) than in the experimental series (once). Clinical observations have suggested that ventricular fibrillation may develop at any instant during a paroxysm of ventricular tachycardia. Every instance of ventricular tachycardia observed in this study was preceded by ventricular premature contractions, occurring either singly, in pairs, or coupled with normal or atrioventricular nodal complexes. The view of a possible progression of ventricular arrhythmias in anesthetized patients, from the innocuous to the serious, would appear to have sufficient basis to justify the application of antiarrhythmia measures against any ventricular arrhythmias.

Arrhythmias must be evaluated not only in terms of their nature, but also in terms of their duration and frequency. In this regard, the longer average duration of ventricular arrhythmias found in the prophylactic series cannot be viewed as an incidental finding. In part, their duration may be explained by failure to institute corrective measures as promptly as in the control series, in order that the effectiveness of prophylaxis, in regard to the persistence of arrhythmias, might be better assessed. In some measure, explanation must also fall back upon the hypothesis that arrhythmias which occurred despite prophylaxis with pronestyl perhaps required stronger provocation, and were hardier, than those occurring in the control series.

In view of the variability in plasma levels of pronestyl attained by combined oral and intravenous prophylaxis, intravenous prophylaxis alone is recommended as being more dependable in the preoperative patient. Intravenous administration circumvents factors which may hinder gastrointestinal absorption in such patients. It is suggested that 500 mg. be administered over 3 to 5 minutes just prior to induction. This may be followed by a like quantity shortly after induction of anesthesia, prior to laryngoscopy and intubation, administered in 2 to 4 minutes. For the additional 1.0 Gm. injected during thoracotomy, divided doses, regularly spaced during the interval required for this part of the surgical procedure, are recommended. If circumstances favor the oral administration of the drug, a blood level usually can be obtained by this route that is within prophylactic range.

Therapy. Pronestyl was found to be uniformly useful in the treatment of ventricular arrhythmias. The drug was administered intravenously in treatment of those arrhythmias which did not respond to ordinary measures, or which responded transiently and recurred as soon as initiating or predisposing factors were reintroduced. Pronestyl regularly abolished the arrhythmias and prevented their recurrence for extended periods of time. Because of the transient hypotension occasionally produced by moderate intravenous doses of pronestyl, an initial scouting dose of 200 mg., in 60 seconds, is recommended for therapy. This may be followed, if required and if no marked hypotension occurs, by 500 mg. doses, in 2 to 4 minutes. If marked hypotension follows the test dose, subsequent dosage should be reduced. The case histories presented serve to emphasize the importance of adequate dosage.

Action of Pronestyl. It is unknown by what mechanism pronestyl influences ventricular arrhythmias. By some means, pronestyl would appear to depress ventricular irritability. Specifically, the refractory period, as measured

by the Q-T interval, is prolonged.

The effect of pronestyl on auricular function appears to be minimal. The high incidence of auricular premature contractions in the experimental series must be regarded as being due to a relative decrease in total number of arrhythmias.

Atrioventricular nodal rhythms were frequently observed to be associated with deep anesthesia in both series. This association has been noted by others and has also been seen in a study of arrhythmias during ether anesthesia now in progress. The development of atrioventricular nodal rhythm is not unusual in cases of anoxia. Further, so-called "escape of the lower centers" is noted in conditions where there is depression of the sinoauricular pacemaker. The unusually high incidence of atrioventricular nodal rhythms during anesthesia would suggest that depression of the normal pacemaker has occurred due to hypoxia or effect of the anesthetic agent, or both.

Factors Associated With The Onset of Ventricular Arrhythmias. In this study inadequate ventilation was the major factor associated with the occurrence of ventricular arrhythmias. It remains to be determined whether it is decreased oxygen or increased carbon dioxide, or both, in the circulating blood and the tissues which is primarily concerned. Toward this end, studies are now in progress.

Reflex mechanisms rarely appeared to play a direct, significant role in the onset of arrhythmias. Perhaps only insofar as these mechanisms contribute to inadequate ventilation may they be considered to be responsible for the initiation of arrhythmias. For example, periosteal stimulation may initiate arrhythmias through reflex brief inhibition of respiration. Similarly, traction on a bronchus may interfere with ventilation, either through a reflex or by direct mechanical interference with respiratory exchange. The observation that the incidence of arrhythmias at the time of laryngoscopy was just as high as the incidence at the time of intubation would appear to be significant. It is at least suggestive that laryngeal and tracheal reflexes are of no greater importance in precipitating arrhythmias than are reflexes from the pharynx and epiglottis.

Arrhythmias of all types have been found to occur in just as many patients during anesthesia with one agent as with another. Kurtz and co-workers reported a high incidence of ventricular arrhythmias during cyclopropane anesthesia, but attributed this to the fact that cyclopropane was their agent of choice in poor risk patients. Since in the series of patients under consideration in the current report, light anesthesia appeared to be associated with the onset of ventricular arrhythmias just as often as deep anesthesia, it would seem unlikely that cyclopropane itself can be held solely responsible for these arrhythmias. The presence of hypoventilation during cyclopropane anesthesia, however, may predispose to the occurrence of ventricular arrhythmias more readily than during anesthesia with other agents. No relationship between the cardiac status of the patients studied and the incidence of arrhythmias was noted.

Since a ventricular arrhythmia may apparently progress from the clinically innocuous to the clinically serious, and since the persistence of any arrhythmia,

particularly a tachycardia, may eventuate in inadequate coronary blood flow, acute coronary insufficiency, and ventricular fibrillation, the importance of its prompt recognition during clinical anesthesia, by an electrocardiographic apparatus, cannot be too strongly emphasized. (Surg., Gynec. & Obst., July '51, S. I. Joseph, M. Helrich, H. J. Kayden, L. R. Orkin & E. A. Rovenstine)

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An Accurate Method for Rapid Blood Grouping of Large Numbers of People

A method for mass blood grouping is presented. The technic used was a slide test, using a single large slide for testing 10 persons at a time for ABO types and Rh factor. The slide used measures 3 inches by 12 inches, made of single-thickness window glass with polished edges. Lines are applied with a silk screen. The slide is divided into 10 units because this is about the optimum number for simultaneous testing. The Clay-Adams viewing box designed especially for blood groupings is used and the large slide is easily accomodated on its illuminated and warmed surface.

For the determination of ABO and Rh blood groups of 400 to 500 persons per day, 2 technicians, 1 recorder and 2 persons to supervise the making of identification cards and keep the line going are required. Only the 2 technicians need be trained personnel. The optimum number of typings per technician per hour is about 50 to 60; this allows a rest period of 5 to 10 minutes once an hour.

On entering the room the line of 10 first meets the assistant technician, who cleans the finger with an alcohol sponge and punctures it with a fresh No. 11 Bard-Parker blade or any other individual sterilized lancet. This is a protection against the danger of contamination of the lancets with the virus of homologous serum jaundice. The cut should be deep enough to produce an immediate flow of blood so that a free-falling drop may be obtained with minimal squeezing of the finger.

The other technician has previously prepared the slide by adding a fairly large drop of saline solution to each of the squares in which anti-A or anti-B serums are to be used; a drop of the appropriate serum is placed in the same squares. The saline solution is added to retard drying of the anti-A and anti-B serums. Serums to be used must be approved (by the N. I. H.) commercial serums of known adequate potency. The anti-Rh (anti-D) serum must be of the so-called "slide-testing" variety. One-tenth cc. of heparin solution is added to each vial of anti-D typing serum. The slide is placed on a white towel under good illumination.

As the donors reach her, the technician notes the number clipped to the clothing of the person to be tested and then, after wiping the finger free of blood with the sponge and squeezing it if necessary to get a small drop of fresh blood, proceeds to set up the typing tests in the appropriate squares. With the end of a wooden applicator stick a very small amount of blood is transferred from the finger to the drop of anti-A serum mixture and stirred to make a fairly

even suspension of blood; the other end of the stick is used to transfer a small amount of blood to the anti-B serum and stir it in. The finger is then squeezed again if necessary, and a large drop of blood is added to the anti-D serum directly from the finger, the finger being guided into position by the technician. The stick is broken in two and one of the broken ends is used to mix thoroughly the blood and the anti-D serum. This mixture should extend from the top to the bottom in a straight-edged pattern, as wide as possible, depending on the amount of blood obtained, but not so wide as to make a thin film that will dry out too quickly.

When the 10 tests are set up, which in the series here reported usually took 4 minutes or less, the slide is transferred to the warmed viewing box. The box is gently tilted back and forth, enough to cause flowing of the blood and anti-D mixtures to the lower part of the square, at intervals of 10 to 15 seconds, until definite agglutination of bloods with the anti-D serum is apparent. Readings are then begun. By this time the anti-A and anti-B serums will have produced definite agglutination of the red cells, if agglutination is to occur at all. As the results are called out, by numbers, they are recorded on the identification card by the recorder, who checks the number on the subject's clothing at the same time. The recorded result is checked, either while being written or afterwards, by the first technician, and also by the second technician, who did the finger stabbing. The identity of the individual is also checked by calling out his name at the time of the checking of the identification card. As an added precaution, persons who are apparently Rh-negative may be asked to wait until after all 10 reports have been given, in order that their Rh tests may be re-examined at the end.

Results of Trials. Twelve hundred and nine presumably healthy subjects, selected at random from 3 hospitals and 2 schools, were typed by the simple slide method outlined above, and the results, as recorded on the identification cards, were compared with the laboratory results of typing by the standard test-tube technics. The latter included "backward typing" (subject's serum against known A and B cells) and two separate Rh tests. Five discrepancies were found. Retesting showed that 2 of these discrepancies were the result of accidental switching of test tubes at the time of venipuncture. In one instance the failure to do "backward typing" resulted in missing a weak Group A by the test-tube method. In another instance the test-tube method indicated as Rh-positive an Rh-negative individual. In only 1 of the 5 instances was the error made by the rapid slide method, an Rh-negative person being incorrectly reported as Rh-positive. The total comparative error was thus 0.33 percent for the tube test results, and 0.08 percent for the rapid slide test.

There were two other errors, which require more detailed comment. It is predictable that any one Rh test will fail to identify some of the low-grade variants of Rh-positive known as D^u. The more sensitive the method and the more potent the typing serum, the fewer will be such errors. Since extremely potent anti-Rh serums are not available commercially and since the Coombs test method cannot well be applied routinely in mass typings, it is predictable that some of these weak variants will be missed in routine typings. In an effort

to determine the approximate frequency of such cases, approximately half (92) of the bloods found Rh-negative by both the rapid slide test and the tube test were further tested with a very potent anti-D by the indirect Coombs test method. One of the 92 proved to be a very low-grade D^u. On this basis it might be expected that approximately 1 percent of those reported Rh-negative might actually be Rh-positive. The frequency of such cases will vary according to the alertness and experience of the technician, since many of these variants give weak reactions by the usual technics. In this connection, one Rh test not reported by the rapid slide-test method (because of very weak agglutination) proved to be a D^u, but was Rh-negative by the tube test technic.

In order to ascertain whether or not fatigue is an important factor in the accuracy of the rapid slide test, a full day's trial run was made. In the course of 7 1/2 hours, 403 subjects were typed and given identification cards. It is quite possible that fatigue would have been an important factor if 500 or 600 people had presented themselves, but it was quite evident that 400 typings were done in a leisurely fashion, without fatigue. (New England J. Med., 21 June '51, F. H. Allen, Jr., L. K. Diamond, & H. J. Madden)

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The Absorption of Enzyme Inhibitors and Antibiotics in Dental Plaques

Many claims in regard to the prevention of dental caries have been made from time to time, particularly in regard to "antiseptic dentifrices" but not until recently was any experimental data available to substantiate the idea.

On the basis of the generally accepted theory concerning the cause and nature of the carious process one should be able to prevent dental caries if the rapid conversion of the residual fermentable sugar in the mouth could be prevented from forming acids. This has been done effectively by the elimination of sugars from the diet and by the use of proper oral hygiene procedures. On the basis of the same theory, it should be possible to prevent acid formation by the proper use of enzyme inhibitors or by directly preventing the growth and metabolism of the microorganisms. The introduction of enzyme inhibitors in the mouth concurrently with fermentable sugars will effectively prevent the formation of acid from the sugar. All efforts to find a substance that will have a prolonged effect, so that when the substance is introduced into the mouth in the morning the effect will be sufficiently persistent to inhibit acid formation from sugars ingested any time during the day, have been uniformly unsuccessful with the exception of the antibiotic penicillin.

It has been found that when many substances that will definitely inhibit acid formation in the mouth are incorporated into a dentifrice, and the dentifrice is used in the morning on arising and in the evening before retiring, they are entirely without effect. Further investigation indicates that when they are introduced in the mouth in this manner, the effect is persistent for only a short period of time, usually about 20 to 30 minutes. When penicillin is used in the same manner, or by means of a lozenge or mouthwash, the effect lasts as long as 24 hours. It is further noted that the morning and night use of a penicillin

dentifrice will cause a persistent drop in acidophilus counts and will actually reduce caries activity as determined by clinical means.

There are many substances as effective as penicillin in their effect on acid production in the mouth and in sugar-saliva mixtures, but as yet none has been found in which the effects persist for such long periods of time. In view of this it was thought of interest to determine the mechanism and cause of this persistent effect and, if possible, formulate substances that would act similarly.

When the conditions that exist in the mouth are considered, it is evident that the retention of water-soluble substances about the teeth would be of extremely short duration unless held to the surface of the teeth by some chemical or physical action. It is known that the fluoride ion will attach itself to the surfaces of the teeth and in many instances may even penetrate the enamel and displace the hydroxyl group from the hydroxy apatite of the enamel substance. There is some indication that other ions may penetrate the teeth, but there is no reason to believe that organic substances such as penicillin could become incorporated in or on the enamel surface. It is known that there is an organic covering sometimes called a film or a plaque which is usually present at least on the inaccessible surfaces of the teeth, and investigation of this material indicates that it is protein in nature. Thus, if an enzyme inhibitor or antibiotic could be made to become absorbed or adsorbed in this surface it might be possible to retain them for considerable periods of time. For this reason the absorption of the various antibiotics and enzyme inhibitors tested by Ludwick, and his co-workers, into protein was measured.

The substances tested by this method consisted of penicillin, streptomycin, bacitracin, tyrothricin, citrinin, menadione, glyceric aldehyde and ammonia. The only one of these substances that was retained and was effective in inhibiting acid formation was penicillin. On the basis of this it would seem that penicillin dentifrice, when used twice a day, will inhibit the growth of lactobacillus in vivo and will inhibit caries activity as determined by the Snyder test by attaching itself to the surface of the tooth, thereby remaining active during the subsequent period of the ingestion of carbohydrates. (J. A. D. A., July '51, L. S. Fosdick, Cdr. W. E. Ludwick, DC, USN & Capt. C. W. Schantz, DC, USN)

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Psychiatric Symptoms Associated With Intracranial Neoplasms

The typical triad of headache, vomiting and papilledema is a late manifestation of intracranial tumor. Early diagnosis of such tumors is necessary, however, if the patient is to obtain the maximum benefit of neurosurgical skill. This is all too often extremely difficult, if not impossible. Early diagnosis becomes even more difficult when the sentinel symptoms seem to be psychiatric, when psychiatric symptoms that develop later obscure the true nature of the disease or when a brain tumor incidentally develops in a person with neurotic symptoms. This is especially true in the absence of papilledema and

roentgenographic abnormalities of the skull. Brain tumors should always be suspected when there is a gradual progressive loss of function of that part of the nervous system contained within the cranium, since headache, vomiting and papilledema are evidences of increased intracranial pressure rather than of a brain tumor per se.

In an effort to delineate the psychiatric manifestations associated with brain tumors the records of 128 consecutive patients with proved intracranial neoplasms seen at the Ochsner Clinic were reviewed. Excluded from this study were patients with metastatic lesions and children under the age of 7 years. Of the 128 patients, slightly more than half (51.5 percent) exhibited psychiatric symptoms on admission to the clinic. Some of these symptoms could be attributed to the effects of cerebral changes produced by the tumors, whereas other symptoms were less definite and seemed to be expressions of the patient's personality before the tumor developed.

In this series there existed a similarity in incidence and nature of psychiatric symptoms exhibited by patients with tumors of the frontal lobe and those of the temporal lobe, with the exception that olfactory or visual hallucinations were manifest in patients with the latter type. In each case, by the time the patients were admitted to the clinic, there was apparent a symptom or sign, such as headache, loss of consciousness, convulsions or aphasia, that should have made the examiner suspicious that the patient's symptoms could not be considered purely psychogenic. This serves to stress the importance of obtaining a complete neurologic and psychiatric history and a careful neurologic examination in such cases.

Particularly difficult at times is the early diagnosis of brain tumors in children because young children are unable to verbalize their symptoms, because headache, irritability or unusual behavior may be considered a behavior problem, and because vomiting may be thought to be due to a gastrointestinal disorder.

Although tumors of the frontal lobe are commonly considered to be associated with psychiatric symptoms with greater frequency than other types of intracranial neoplasms, it must be pointed out that such symptoms are associated with tumors of the temporal lobe just as often. However, tumors of the frontal lobe anterior to the motor areas often do produce subtle peculiarities in the patient's personality that are insidious in onset. Other psychiatric manifestations, produced by frontal lobe tumors, appear gradually; these include impairment of memory (perhaps at first considered as absent-mindedness but later becoming a more obvious and serious memory defect), difficulty in concentration, a flattening of the affect coupled with a growing apathy regarding domestic and commercial affairs, carelessness in personal appearance and use of obscene and facetious speech. Some degree of apraxia may also develop in such patients. However, for the purposes of this study apraxia, aphasia, and related conditions have not been considered as truly psychiatric symptoms and patients showing such manifestations in the absence of other psychiatric symptoms were not included in the present series. It is important not to mistake apraxia, aphasia and such related conditions for conversion hysteria or for the blocking seen in schizophrenia.

Neoplastic lesions of the temporal lobe are notorious for causing hallucinations, which may be visual, olfactory or gustatory. Visual hallucinations

typically are "formed," that is, visions of objects, but there may be exceptions. For example, one patient with a tumor of the temporal lobe had a "nervous breakdown" a few years before being seen and "unformed" visual hallucinations (flashes of bright lights) for 1 year. Gustatory hallucinations consist in peculiar tastes and olfactory hallucinations are peculiar odors that are usually described as unpleasant and likened to the odor of burning tar, asphalt, crude oil, gas or cooking cabbage. These types of hallucinations may be associated with dreamy states and uncinate fits. In such attacks, things seem unreal and distorted to the patient; sometimes strange things seem familiar and at other times patients describe the feeling as if one has been in a dream. The dreamy state may be followed by a generalized epileptiform convulsion. Of course, tumors of the temporal lobe may cause aphasia.

Other locations involved more rarely that at times pose diagnostic problems are the occipital lobe and third ventricle. Patients suffering from tumors of the occipital lobe may complain of visual hallucinations that are not "formed," that is, they may see flashes of light or color. Ball-valve tumors of the third ventricle in which the severe headache may be quickly relieved by changing the position of the head, because of the latter fact, must not be mistaken for conversion hysteria. Hypersomnolence may be produced by tumors involving the floor of the third ventricle; such somnolence is frequently mistaken for narcolepsy or hysteria. Such patients may fall asleep while driving automobiles, while eating, or at other inappropriate times. Also, diencephalic autonomic epilepsy caused by tumors in this region must be clearly distinguished from purely psychogenic disorders, which such a condition might resemble. (Am. J. Psychiat., July '51, T. L. L. Soniat)

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Iatrogenic Disease

The word "iatrogenic" is derived from the Greek words, iatro, meaning physician or therapy, and genesis, meaning creation. Iatrogenic disease, therefore, is disease created by the physician, or broadening the meaning somewhat, disease aggravated by the physician.

Within the past 25 years, with the incidence of illness resulting from two world wars, realization has come that many diseases stem from disturbed physiology rather than disturbed anatomy. Generally speaking, such functional disturbances arise from some emotional upset, such as insecurity, fear, anxiety and unhappiness in the life situation. Many organic diseases have their origin in disturbed emotional states. Chief among them are peptic ulcers, essential hypertension, rheumatoid arthritis, asthma and other allergic states and dysmenorrhea. In the light of the high emotional content of these diseases, it is easy to see how a doctor's own emotional reactions to his patient's disease may influence the patient's reaction to his symptoms. What a doctor tells his patient also has great influence.

Doctors are guilty of many specific practices that tend to create invalidism and aggravate existing disease. On careful physical examination, some abnormality

can be found in nearly everybody. Many times, because no definite pathologic condition can be found, the symptoms are attributed to some trivial abnormality. These trivial findings may lead one to prescribe much needless therapy.

Many a thyroid gland has been removed because of a rapid pulse and an erroneous basal metabolism test. Surgery does not relieve symptoms that are due to a psychoneurosis. Further, in such cases, there is the ever-present danger of creating hypothyroidism with all its woes. Cystic ovaries, malposition of the uterus and slight thickening of the fallopian tubes often lead to needless surgery. Again, when a patient's dysmenorrhea is due to psychogenic causes, and when her backache is due to fatigue or flat feet, surgery will be of no benefit. Furthermore, such surgery often leads to an early menopause.

Probably the worst thing that surgeons do is to operate unnecessarily for adhesions and so-called "chronic appendicitis." One young girl had a definite situational psychoneurosis that caused many vague gastrointestinal symptoms. Her surgeon, without paying any attention to her emotional make-up, removed her "chronic appendix." As the symptoms persisted, she subsequently had two more operations for "adhesions," neither of which brought relief. Her illness persisted more than 5 years. She was cured only when marriage brought an end to her unhappy situation.

Chronic alcholism always presents a problem. Nearly all alcoholics demand some sort of sedation for their hang-overs. Usually, one of the barbiturates is prescribed. Many such patients, as a result of the indiscriminate use of these drugs, have become barbiturate addicts.

Asthma presents another problem. A large number of asthmatic patients have become narcotic addicts because doctors prescribe morphine and other narcotics too freely. Fortunately, that danger is now realized, and addiction from that cause is relatively infrequent.

Probably the greatest harm is done in dealing with cardiovascular disease. The layman hears of the comparatively few sudden deaths due to coronary thrombosis and to cerebral hemorrhage. He hears nothing of the cardiac victims who live on, year after year, with chronic congestive failure, or of the arteriosclerotic patients who gradually fade away with nephritis and heart failure. Consequently, to his mind, heart disease and high blood pressure are causes of sudden death and are greatly to be feared.

Many patients have had the label "nervous heart" put upon them when the doctor could find nothing more than a simple tachycardia to explain the symptoms. In such a case it would be better to tell the patient definitely that he has no heart disease and to try to explain the mechanism behind his symptoms. In dealing with actual heart disease, it is easy to make a cardiac invalid by telling the patient that he has angina pectoris, or that he has a heart leak. Rather, one should tell him clearly what he has, what the danger signs are, and what is likely to produce those signs. Be specific! Tell him to learn his load limit, stay under it, and forget about his heart.

The layman knows that digitalis is a heart drug. When it is prescribed for him, he knows that he has heart disease. The indiscriminate use of this drug, therefore, is to be deplored. Its indications are relatively few and well defined.

It should never be used without definite indication.

Victims of hypertension constitute a terrific problem. Except for the aged arteriosclerotics, these people are "eager beavers." They are also likely to be worriers. It doesn't help one of these patients to be told: "My goodness! Your blood pressure is 220. It's a wonder you got here without having a stroke!" It would be better to prescribe the proper medicines, explain his disease, stressing the point that he is not likely to have a stroke, and offer reassurance.

Much harm can be done by giving alarming information. One of the author's patients had an episode of acute anxiety because he was told that he should have an operation for his stomach ulcer, because ulcers in the location of his sometimes become cancerous. Even a doctor's facial expression may alarm a patient. If, in taking a blood pressure, the doctor looks surprised and concerned his concern is immediately transmitted to the patient. If fright caused by physical findings or an unexpected event is shown, the patient is immediately made worse. Imperturbability and a poker face are absolute essentials in good medical practice.

Anxiety may also be aroused by too many office visits. Seeing a patient two or three times a week for his blood pressure does not help him, and, in all probability, serves to focus his attention more on his complaints. Seeing him too often may make him think he is much sicker than he really is.

The science and art of medicine is so great that no one doctor can master all of it; therefore, the doctor sometimes errs through ignorance. Sometimes he is so pressed by work that he doesn't take time for adequate explanations and instructions. Many a self-made diagnosis is confirmed by a doctor because the patient seems to demand it and the doctor fears that the patient will go to someone else unless he concurs.

There is no set procedure for preventing the iatrogenesis of disease. Since every patient is a law unto himself, it behooves the doctor to study each one carefully, and be discreet in what is said to him.

It is urged, "If you can do no good, be sure you do no harm." Oliver Wendell Holmes is quoted, "The best doctor is the best inspirer of hope." (North Carolina M. J., June '51, J. H. McNeill)

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A Study of the Exfoliative Cytology in Patients With Carcinoma of the Oral Mucosa

Since the use of the cytologic smear has become so popular as an aid in diagnosis of carcinoma of the cervix, uterus, and certain other areas of the body, it seemed logical that the method might also be useful in the study and diagnosis of carcinoma of the oral cavity. For this investigation 15 patients with oral carcinoma were chosen and cytologic smears were prepared from the lesions and the 6 normal areas of the mucosa according to the technic described by Montgomery. These smears were fixed and stained by the method outlined by Papanicolaou and Traut. Differential counts of the types of epithelial cells found were made and a detailed study of the individual cells obtained from the lesion was undertaken.

It is interesting to note that all these patients were white and with one exception they were men. Their ages varied between 57 and 94 years. The duration of the lesions varied between 2 months and 16 years, although some of the data are vague and unreliable. The regions most frequently involved were the mucosa of the cheek, the lower lip and the mucosa of edentulous ridges. Nine patients showed lymph node metastasis at the time they came under the author's observation. Biopsies were performed in 12 cases; 11 showed squamous cell carcinoma. One patient refused surgery, 2 others were considered far advanced and inoperable; 5 patients had been treated previously by surgery or irradiation before the authors had the opportunity to examine them.

Statistical comparison of differential counts from normal areas in these mouths of patients with corresponding areas of healthy individuals was done by the Statistics Laboratory of Ohio State University, using a formula similar to that applied in the study of leukoplakia. Similarly, the normal areas of the mouths of cancer patients were compared with the normal areas of patients with leukoplakia.

There is no evidence to show that normal areas of the mouth in patients with oral cancer differ from corresponding areas of the mouth of normal subjects. There was no significant difference between the normal areas of the mouths of patients with cancer and those with oral leukoplakia except possibly a slight increase in the number of yellow cells in the palate and anterior portion of the tongue in patients with leukoplakia.

The cellular distribution in normal and diseased areas of the mouths of the cancer patients was compared. All 13 patients exhibited significant differences between normal and diseased areas, and in all but 2 of these the number of blue cells in the diseased areas was less than in the corresponding normal areas.

A detailed study of individual cells in the smears from the malignant lesion was undertaken in order to explore the morphologic characteristics of malignant cells in oral cancer. The qualitative evaluation of malignant cells, in fact their recognition and differentiation from benign cells, depends upon certain criteria which can be found in the nucleus as well as in the cytoplasm. An abnormally large nucleus with a definitely disturbed nuclear-cytoplasmic ratio is perhaps one of the characteristics of malignancy of the oral cavity most frequently found. Cells showing these criteria were present in 14 of the 15 cases. Hyperchromasia proved less reliable as a characteristic; as it was present in only 9 cases. A thickened nuclear membrane, which is stressed by Gates and Warren as another characteristic of malignancy, was found in only 3 instances. Alterations in the nucleolus take a prominent place in the diagnostic features of malignant cells. Abnormally large nucleoli were found in 13 cases; oval, lance-shaped, or dumbbell shaped nucleoli were found in 11 cases and in 8 cases the nuclei contained more than 1 nucleolus. Other nuclear inclusions, which neither belong to the chromatin network nor behave tinctorially like a nucleolus, were found in 7 cases. They resembled either the inclusion bodies of Lipschutz (acidophilic degeneration) or were vacuoles filled with a lighter-staining basophilic material. Mitotic figures, either normal or abnormal types,

were not seen in these cytologic smears. This fact may well be explained by the nature of the smears, which include only the superficial cells of the neoplasm.

Changes in the cytoplasm were less frequent and less characteristic. The most reliable sign of malignancy in the cytoplasm consisted of an altered staining behavior with the Papanicolaou stain. Cells which had the morphologic appearance of the blue cells stained brilliantly red or even bright orange, and gradual transitions between the various color tones, which are a prominent feature of the normal smear of the oral cavity, were often absent. In 9 cases the cytoplasm contained clear vacuoles. In 9 others inclusion bodies were found. In 7 cases the cytoplasm of the malignant cells showed marked phagocytic properties. Bulky and grotesquely shaped cells were present in 11 cases, although they never were very numerous and could have been overlooked easily by less careful studies. Nine cases showed small, deeply basophilic staining cells with extraordinarily large nuclei. When present, they gave reliable evidence of a rapidly growing and less differentiated neoplasm. Although these cytologic studies were conducted on rather well-established clinical cases, and in some instances quite sizable lesions, 7, or nearly 50 percent, of these cases did not furnish the number or variety of malignant cells which the clinical appearance would lead one to expect. Smears from the necrotic areas of the large ulcerative lesions revealed an abundant amount of amorphous material together with bacteria and pus cells, but malignant cells were found only upon careful search. If the smears were taken from the margin of the crater, malignant cells were often equally sparse and were crowded out by normal epithelial cells, making the correct diagnosis much more difficult. For this reason it is recommended that smears be taken from the center of the lesion, although the cytologic epithelial material is less abundant. In 9 of the cases smears taken from this area showed only a few normal epithelial cells. An increased number of pus cells was found in 12 cases studied, and red blood cells were present in 10. An attempt to go beyond the simple diagnosis of malignancy and to draw certain conclusions as to the degree of differentiation and the rate of growth was not successful.

A comparison of the unaffected areas of the oral mucosa in the cancer patients with corresponding areas of healthy individuals showed no qualitative cytologic differences.

In 13 of 15 cases a cytologic diagnosis of malignancy could be made without too great an effort, from smears taken from the lesion. Usually the malignant changes were discovered after careful examination of a single slide, and other slides from the same lesion gave identical patterns. In 2 cases repeated smears showed very scant cytologic material and cells bearing criteria of malignancy were extremely scarce. Without the clinical picture, the diagnosis of malignancy in both cases would not have been made. This may have been the fault of the technic, particularly the method of obtaining the smear. This series of cases is too small to give the two "false negative" smears any statistical significance. (J. Dent. Research, June '51, P. W. Montgomery & E. von Haam)

Radiation Damage to Normal Tissues in the Diagnosis and Treatment of Nonmalignant Conditions and its Surgical Repair

Irradiation in the form of either radium, x-ray or isotopes, is a valuable procedure in the treatment of disease. It is not, however, without its dangers and should always be administered by an expert.

There is a great difference between using irradiation in treating cancer and in using it to treat benign conditions. In cancer, one is justified in taking great risk of damage to normal tissues, as the one consideration is to destroy the cancer. The trained radiologist has learned to treat many cancers successfully with a minimum damage to normal structures. In benign conditions, one must be sure that the resulting cure is not worse than the disease. There is no justification for causing permanent damage to other tissues when treating benign conditions. Irradiation in malignant conditions is effective because those cells that are immature and more rapidly growing are more sensitive to radiation. The greater the number of undifferentiated cells, the more radiation-sensitive is a tissue.

This paper deals with the unexpected and unwanted effects of irradiation in the treatment of benign conditions. It is a well known fact that the unwise or inaccurate use of irradiation will cause cancer. Here, then, is a weapon used for treating cancer that if used unwisely in benign conditions will produce more cancer. These changes may not occur for a decade or two, but in one case cited by the author the cancer appeared in 2 1/2 years.

Low-voltage x-ray or unscreened radium has been the offender in the greatest number of cases of irradiation damage to the skin. High-voltage x-ray may produce untold damage to normal structures, but there is usually a total destruction, and the same problem of cancer causation is probably not involved. The author has rarely observed the occurrence of cancer in areas treated by high-voltage x-ray and believes that if proper filters are used cancer will not occur.

Wolbach, as long ago as 1909, described the pathologic characteristics of chronic radiodermatitis. In 1924, in another study, he summarized the changes in the skin: complete loss of the appendages of the epidermis, replacement of the normal collagen by a peculiar dense hyaline collagen, obliterative processes in blood vessels of the corium and subcutaneous tissues, necrosis of varying size in the corium, at first in the region of thrombosed telangiectases and reparative proliferation of the epidermis. He further outlined the gradual evolution of a carcinoma in such an area. He also pointed out that changes by irradiation are progressive and irreversible.

In an area of radiation damage there is usually definite loss of subcutaneous fat; this is greatest in the center of the radiated area. When ulceration occurs little, if any, underlying fat remains in that portion of the damaged area. If there is deeper destruction it extends to the fascia, which has a poor blood supply and is easily destroyed.

In the surgical treatment of damaged tissues from irradiation certain facts should be borne in mind:

(1) As much damaged tissue as possible should be removed, down to normal structures. (2) If no fat remains, thin skin grafts will not be entirely successful and are not as satisfactory as pedicle flaps containing fat. In surgical treatment of fingers thick split grafts are best for good functions, but there is always the likelihood of focal areas of destruction in the grafts. (3) Wounds from removal of radiated tissue should never be left open to granulate. If such wounds are left open they will soon be covered over by a "scum" of avascular pseudohyalinized tissue, whether the irradiation was given a year before or twenty years before. All such wounds should be covered at once. (4) If there has been deep destruction down to fascia, periosteum or bone, a healthy base may be unobtainable. If the skin and fat of the periphery are normal it is possible to rotate a pedicle flap to cover such a wound, even though the base is very bad. Nourishment to the flap is furnished from the skin edges. Gradually the flap will adhere to the underlying tissues.

X-radiation should be used only by, or under the supervision of, a well trained physician. Repeated doses of low-voltage therapy with improper screening cause permanent damage to tissues. This damage may lead to the development of cancer in the treated area.

Irradiation should not be used when surgery will accomplish as good a result. It should be avoided in all benign conditions except plantar warts, particularly in the young. It should not be used in benign conditions over the epiphyses of growing bones. It should never be used in the treatment of benign moles. In the treatment of infections or skin diseases, it should be used only by an expert.

X-radiation is probably a safe method of treatment for plantar warts, if used wisely. It is never safe to use it a second time. Patients should be told this, so that they will not apply to various physicians for further treatment. Care should be taken that the treated area does not become traumatized or infected. (New England J. Med., June 28'51, E. M. Daland)

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Ocular Complications Encountered in Intracranial Arteriography

Intracranial angiography, the roentgenographic examination of the skull following the perfusion of intracranial vessels, provides an excellent means of obtaining diagnostic information. However, it is not without danger. Complications, such as pain, arterial spasm, allergic phenomena, thrombosis, emboli, convulsions, hemiplegia, exacerbation of existing symptoms and even death, may be encountered. Weekers reported a case of occlusion of the right temporal retinal artery following injection of the right internal carotid artery with 20 cc. of iodopyracet solution ("umbradil"). The patient also presented a convulsive seizure and left hemiplegia.

The observation that patients who had had intracranial angiography exhibited facial and conjunctival petechiae postoperatively on the homolateral side instigated the present study of the frequency and type of ocular complications

encountered in 80 patients undergoing intracranial angiography at the University of Michigan Hospital.

Ocular complications were encountered in 86.3 percent of the patients. One death, secondary to thrombosis of the internal carotid artery, followed the procedure.

Petechial hemorrhages were frequently observed in and about the homolateral eye and adnexa in the 80 arteriographies. Conjunctival petechiae, especially in the fornices, were almost a constant feature; they could, in some cases, be visualized almost immediately on completion of the perfusion of the iodopyracet. In other patients the hemorrhages were not visualized until 30 to 90 minutes after operation. It is believed that there is some correlation between the frequency and severity of the petechiae and the amount of the contrast medium injected. The majority of the retinal hemorrhages were round, granular and, in a few cases, preretinal. Most were confined to the posterior pole. Many of the hemorrhages presented white centers, and in many cases cotton-wool exudates also.

Severe optic neuritis was encountered in 1 patient, with eventual complete loss of vision. Temporary visual loss (10-30 minutes) was observed in 2 patients, with subsequent return to normal. The homolateral pupil was temporarily dilated in 5 patients, with return to normal within 3 to 24 hours. Pain in and about the eye was a complaint of 2 patients.

The records of 457 patients undergoing intracranial arteriography (1941-1950) were reviewed for the occurrence of sequelae of a serious neurological nature. Four patients became seriously comatose; 6 had hemiplegia or hemiparesis and 6 experienced convulsions. On introduction of the needle, spasm of the carotid artery was met twice. (A.M.A. Arch.Ophth., June '51, H. F. Falls, R. C. Bassett & A. E. Lamberts)

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Pyrabenzamine Cream in Portuguese Man-of-War Stings

Commander D. F. Hottenstein, MC, USN, reports favorably the local use of 2 percent pyrabenzamine cream as treatment for stings from the "Portuguese man-of-war". The cream was massaged into the affected areas with immediate relief of pain and burning. This method of treatment is published for information and possible use in similar cases.

Refer BuMed News Letter vol. 1, no. 4 (16 April 1943) and United States Naval Medical Bulletin, vol. 1, no. 2 (March 1943), relative to the use of calcium gluconate intravenously in such cases. (Ed.)

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From the Note Book

1. Brig. Gen. J. Cooney, radiation safety advisor to Joint Task Force 3 has stated that "experience in recent test programs repeatedly has demonstrated that radiation hazards will not delay rescue and recovery work after an air burst of an atom bomb. The immediate radiation hazard from the air burst disappears after the first 2 minutes. Rescue, fire fighting and recovery work can begin immediately in any area where there is life, as in any major catastrophe caused by conventional air attacks, earthquakes or disasters on the scale of those at Texas City and Halifax." (Government Services, U. S. Atomic Energy Commission, J. A. M. A., 7 July '51)

2. The U. S. Naval School of Aviation Medicine became a "Command" on 5 July 1951. Captain L. D. Carson, MC, USN, assumed command of the school following commissioning ceremonies held in the station auditorium. (PIO, School of Aviation Medicine, Pensacola, Fla.)

3. Twenty-one hospitals operated by the Public Health Service under the name "U. S. Marine Hospitals" were redesignated U. S. Public Health Service Hospitals on 1 July 1951. The hospitals affected by the change in name are located in ports along the ocean and gulf coasts, the Great Lakes and the Mississippi River. In addition, there are 2 tuberculosis hospitals at Fort Scranton, N. Mex., and Manhattan Beach, N. Y., and the Carville, La., Hospital for treatment of leprosy. (FSA, PHS News Release, 30 June '51)

4. There are 2,267 public venereal disease clinics in the United States, Alaska, Hawaii and Puerto Rico. A 157 page directory carrying names and addresses of each diagnostic and treatment facility, as well as summaries of prenatal and premarital laws, laboratory facilities in each state and lists of hospitals and facilities for American seamen, has been published by the Public Health Service. (FSA, PHS News Release, 3 July '51)

5. The total cost of the British National Health Service program for 1950 was 451,000 pounds sterling. Hospital services cost 267,000 pounds, approximately 59 percent of the total costs. General medical services cost 48,300 pounds, a little more than 10 percent of the total cost. No estimate is available of the total medical services rendered by general practitioners, except that it is considerably more than 10 percent. (Editorial, "Remuneration in Great Britain," GP, July '51)

6. Processes for producing X-ray photographs in color have been independently discovered by Dr. G. E. Donovan, of Swansea, Glamorgan, Wales, and Dr. Everett L. Pirkey, Professor of Radiology at the University of Louisville, Ky. Samples of films, reproduced in the 21 July issue of Collier's, are of startling clarity and brilliance. This development should prove to be of enormous importance, both as training aids for students and general practioners, and in the

development of new discoveries in diagnostic technics. (Sey Chassler, "What Color X-Rays Can Do," Collier's, 21 July 1951)

7. Chloromycetin suspension in saline solution, if injected intramuscularly in adequate dosage, is apparently an extremely effective preparation in the treatment of granuloma inguinale. (J. Ven. Dis. Inform., July '51, F. W. Harb, W. G. Simpson & C. E. Wood)

8. Problems in cardiovascular surgery are discussed under the headings of: (1) those in which surgery may accomplish good or excellent results; (2) those in which surgery may bring about moderate improvement and (3) those in which surgery is of doubtful value or suitable methods are not yet fully developed. (J. Thorac. Surg., June '51, A. Blalock)

9. "A Survey of the Chewing Ability of Denture Wearers" appears in the Journal of Dental Research, June 1951. (R. S. Manly and P. Vinton)

10. A new method for the prevention of anaphylactic serum reactions is discussed in the Journal of the International College of Surgeons, June 1951, by G. Wolfsohn.

11. Ground breaking ceremonies for the Armed Forces of Pathology building were held at the Army Medical Center, Washington, D. C., on 10 July 1951. The structure, requiring 2 years to build, will be bomb resistant. Three of the 8 floors will be underground. (Washington Post, 10 July 1951)

12. It is expected that in the year 1951, 50,000 persons will be killed in automobile accidents and 1,500,000 will be injured. A large number of the injured will have fractures of the facial bones. (Editorial, "Smashed Faces," GP, July '51)

13. Hypertrophic osteoarthropathy, as the first significant symptom of bronchogenic carcinoma, is discussed in the Journal of the American Medical Association, 30 June 1951, by J. D. Pattison, E. Beck and W. B. Miller.

14. "Half a Century of Progress in Orthopedic Surgery", from 1900 to 1950, is fascinating reading. (British volume, J. Bone and Joint Surg., Nov. '50)

15. The volume of the circulating red cell mass during pregnancy and the puerperium determined by direct measurement, using radioactive red cells, is discussed in American Journal of Obstetrics and Gynecology, June '51, W. L. Caton et al.

16. The World Health Assembly opened in Geneva on 7 May and met for 16 days under the chairmanship of Dr. Leonard Scheele, Surgeon General of the U. S. Public Health Service. Seventy countries and 20 international organizations participated in the meetings. The most important achievement of the Assembly Legislative Body was the adoption of international sanitary regulations which will automatically come into force on 1 October 1952. (Medical News, J.A.M.A.,

30 June 1951)

17. "The Cutaneous Toxicity and Therapeutic Effectiveness of Penicillin O" is discussed in New England Journal of Medicine, 5 July 1951, by R. R. Marsh and I. G. Tillotson.

18. A preliminary report on the use of potassium gluconate in hypopotassemia appears in Science, 29 June '51, A. Bernhard.

19. A portable humidifying unit in the treatment of tracheobronchial inflammation is described in A. M. A. American Journal of Diseases of Children, June 1951, by R. M. Smith and R. Denton.

20. "A Review of New Drug Therapies in the Treatment of Alcoholism" appears in the New England Journal of Medicine, 21 June 1951, J. Thimann.

21. The management of cancer of the middle ear and mastoid is discussed in A. M. A. Archives of Otolaryngology, June 1951, W. L. Mattick and J. W. Mattick.

22. For the week ending 7 July 1951, a total of 407 cases of poliomyelitis was reported, representing an increase of 19 percent over the previous week's figure of 341. For the same week last year, 478 cases were reported. The cumulative total for the calendar year is 3,239, as compared with 3,656 last year. No section of the country showed a marked increase in cases for the current week as compared with the previous week. (FSA, PHS News Release, 12 July '51)

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Course in Dental Material Research

A vacancy exists in the Course in Dental Material Research as described in paragraph 9 of BuMed Circular Letter 51-19, of 26 January 1951. Applications are desired from interested Regular Navy dental officers, preferably in the grades of lieutenant or lieutenant commander.

Letter requests to attend this course, which commences September 17, 1951, should be forwarded to the Chief of the Bureau of Medicine and Surgery, (Attention: Code 611) prior to 15 August 1951. (Dental Div., BuMed)

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BUMED CIRCULAR LETTER 51-100 27 June 1951

From: Chief, Bureau of Medicine and Surgery
To: All Medical Department Activities and Facilities

Subj: Requisitioning, receipt procedures, stock levels, emergency expansion reserves, and priority indicators for medical and dental stores

Ref:
(a) BuMed Cir. Ltr. 50-101
(b) BuMed Cir. Ltr. 50-73
(c) Art. 23-130, Manual of the Medical Department
(d) SecDef memo of 22 Nov 1950 to Secretaries of the Military Departments
(e) BuMed Cir. Ltr. 50-28
(f) Par. 23004, Vol. II, BuSandA Manual
(g) Par. 23101, Vol. II, BuSandA Manual

Encl:
(1) Preparation and Submission of BuMed Material Requisition, NavMed Form-4
(2) Procedures to be Employed in Requisitioning Nonstandard Medical and Dental Supplies and Equipment
(3) Levels of Supply for Medical and Dental Stores
(4) Emergency Expansion Reserve Reporting Procedures - Applicable only to Continental Shore Stations Having Medical and/or Dental Facilities
(5) Procedures for Receipt of Medical and Dental Supplies and Equipment Direct from Contractor when Charged to Medical Stores Allotment of the Bureau
(6) Priority of Requests for Medical and Dental Materials

References (a) and (b) are hereby cancelled and superseded by enclosures (1) through (6). Reference (c) is no longer applicable in its present form and will be revised in a subsequent change to the Manual of the Medical Department.

This letter, with enclosures, which will not be printed in the Navy Department Bulletin, states in detail the procedures necessary for requisitioning, receipt procedures, stock levels, emergency expansion reserves, and priority indicators for medical and dental stores.

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BUMED CIRCULAR LETTER 51-101 28 June 1951

From: Chief, Bureau of Medicine and Surgery
To: Commandants, Naval Districts, Continental United States
Commanders, Naval Training Centers
Commanding Officer, Naval Training Station, Newport, Rhode Island
Commanding Generals, Marine Corps Recruit Depots
Superintendent, Naval Academy, Annapolis, Maryland

Subj: Tuberculin testing and chest X-ray findings

Ref: (a) BuMed Cir. Ltr. 51-27
(b) Par. 21103, ManMedDept, 1945

1. Reference (a) shall be amended by substitution of "Marine Corps Recruit Depots" for "MARCORPSBAKS" in the "To" line.

2. The following shall be substituted for subparagraph 6c of reference (a) to bring it into conformance with the National Tuberculosis Association's 1950 edition of "Diagnostic Standards and Classification of Tuberculosis:

"c Result of Test (see NOTE in preceding paragraph).--

The test shall be examined after an interval of not less than 48 hours nor more than 72. Redness without induration does not constitute a reaction. Reactions are to be graded as +, ++, +++, ++++, "doubtful", or "negative", depending upon the extent of induration measured at its widest diameter, as follows:

(+) Definite induration more than 5 mm. and not exceeding 10 mm. in diameter.

(++) Induration measuring from 10 to 20 mm. in diameter.

(+++) Induration exceeding 20 mm. in diameter.

(++++) Severe induration and an area of necrosis.

("doubtful") A reaction with a trace of induration measuring 5 mm. or less in diameter.

("negative") Redness without associated induration does not constitute a reaction, and should be reported as negative."

3. There is need for correlating the results of tuberculin tests and chest X-ray examinations.

a Of 99 individuals admitted for active pulmonary tuberculosis during 1949 whose "negative" recruit photofluorograms were available for review, 12 percent had technically unsatisfactory recruit films, and the films of 15 percent contained definitely suspicious findings in the region where disease was later reported.

b Only approximately 10 percent of recruits react positively to the tuberculin test.

c The great majority of recruits with active tuberculosis will be among those whose tuberculin test is positive.

4. In view of the findings mentioned in paragraph 3, it is directed that addressees shall arrange for a second reading of the photofluorograms of recruits whose tuberculin tests resulted in doubtful or positive reactions. When, as a result of such reviews, re-examinations are made on 14 x 17 inch film, the appropriate Photofluorographic Log (NAVMED-1161) entries (column labelled "Film Interpretation") shall be corrected with red ink.

5. Recruits received from Armed Forces Induction Stations who have doubtful or positive tuberculin test reactions shall receive another chest photofluorographic examination. The interpreter of photofluorographic film shall be informed of the reason for the examination. This constitutes a modification of that portion of paragraph 21103.1 of reference (b) which states "a recruit who has received roentgenographic examination of the chest during his physical examination for enlistment or induction with negative findings does not require another roentgenographic study upon arrival at a naval training station or Marine Corps recruit depot."

6. Tuberculin testing should be accomplished as soon as practicable so that shipment of films to this Bureau will not be unduly delayed.

7. With each shipment of films and reports submitted to this Bureau, the following statement shall be inserted on the appropriate Photofluorographic Log, NavMed-1161 or 1161(a)--:

"All recruits reported above have received a tuberculin test and the provisions of paragraphs 4 and 5 of BuMed Circular Letter No. 51-101 have been complied with".

H. L. Pugh

The above letter will not be printed in the Navy Department Bulletin.

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BUMED CIRCULAR LETTER 51-102 28 June 1951

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Quarantine of dogs and cats brought into the Panama Canal Zone

Ref: (a) Supplement No. 18 to the 1947 Pamphlet, Panama Canal Navigation Regulations, dated 20 April 1951

1. The Isthmus of Panama, including the Canal Zone, has been free from rabies for more than 35 years. In the interest of maintaining this favorable situation, the Acting Governor of the Canal Zone has promulgated reference (a) which is quoted as follows:

"Regulation 119pp.1. Quarantine of dogs and cats; quarantine period. Every dog or cat brought into the Canal Zone from off the Isthmus shall be held in quarantine, under veterinary inspection, for a period of not less than four months."

2. The present charge to the animal's owner during the quarantine period is fifty cents (50¢) per day, which includes board and veterinary services.

C. J. Brown
Acting

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BUMED CIRCULAR LETTER 51-103 29 June 1951

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Instructions relative to material to be reported as Equipment, Plant Property Class 3 and material to be carried and accounted for as equipment

Ref: (a) BuMed Cir Ltr 49-140; NDB Jul-Dec 1949, 49-769, p. 118
(b) BuMed Cir Ltr 49-141; NDB Jul-Dec 1949, 49-770, p. 121
(c) Paragraph 63003-3, 63003-5 and 63003-6 Revised BuSandA Manual

Encl: (1) List of Medical and Dental items to be reported in the Plant Account (Property Class 3)

References (a) and (b) are hereby cancelled and superseded by this letter.

This letter, with enclosure, contains detailed instructions for accounting of material reported as Equipment, plant property Class 3 and material carried and accounted for as equipment.

BUMED CIRCULAR LETTER 51-104 3 July 1951

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Routine roentgenographic examinations of the chests of dependents of naval personnel

Ref: (a) Paragraphs 415 through 419, Manual of the Medical Department, 1945
(b) Paragraph 21103, Manual of the Medical Department, 1945

1. Whenever practicable, dependents of naval personnel, age 15 years or older, should receive routine roentgenographic examinations of the chest at approximately the same occasions and time intervals as naval personnel, on a facilities available basis. The equipment and techniques specified by reference (b) shall be used.

2. The results of the examinations shall be recorded and forwarded as required by reference (b) with the following modifications:

a. Photofluorographic Logs. Enter the letter "D" after the appropriate photofluorogram number on forms NavMed 1161 and 1161(a). Enter the individual's full name and date of birth, and the interpretation of the film. A record of the addresses of the individuals concerned should be maintained at the station where the examinations are made.

b. Identification of film. The letter "D" should appear on the film, after the film number.

c. Report of Photofluorographic Chest Survey. A separate form NavMed 618 for dependents shall be completed as far as possible and forwarded with each roll or package of films. Upon the reverse of the form or upon an attached sheet of paper, enter the photofluorogram numbers of individuals re-examined on 14 x 17 inch film. Place an asterisk before the appropriate number when the re-examination resulted in recommendation for further clinical study.

d. Individual reports. Individual reports of re-examinations on 14 x 17 inch film are not desired.

3. The purpose of these examinations is to increase the efficiency of tuberculosis control among naval personnel and to cooperate with civil authorities concerned with tuberculosis control in the communities where the dependents of naval personnel reside. It is therefore important, if X-ray surveys are undertaken, that the participation of dependents in routine chest X-ray examinations be as complete as possible, and that follow-up studies to determine the nature and extent of defects disclosed be as prompt and thorough as circumstances permit.

When tuberculosis in communicable form, or other communicable disease, is discovered, civilian public health requirements shall be complied with and effort made to determine where the disease was contracted and the contacts to whom it may have spread, especially those in the naval service.

4. Nothing in this letter should be construed as modifying present policies concerning medical care of dependents.

H. L. Pugh

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BUMED CIRCULAR LETTER 51-105 12 July 1951

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Manual of the Medical Department and Bulletin of Bureau of Medicine and Surgery Circular Letters; distribution policy for

1. Past policy.--In the past, personal copies of subject publications were automatically provided to all Medical Department officer personnel on active duty. In addition, ship and station office copies were furnished upon request to activities having Medical Department personnel aboard.

2. New policy.--The distribution of personal copies is being discontinued. All presently issued personal copies shall be returned to the Bureau or assigned as office copies if required. Effectively immediately, the following policy will apply:

a. Office copies.--Ship and station office copies will be furnished upon request to those activities having personnel of the Medical Department of the Navy aboard and to those other Navy and Marine Corps activities having a stated need for same. These two publications are normally issued as a set. The Bureau will assign the copies, and automatically forward changes thereto, to the commanding officers of the ships and stations and not to departments or offices within the activity. It is important that all activities establish rigid internal distribution and maintenance controls to assure that all assigned copies are necessary and maintained in a current status.

b. Personal copies.--When the Manual of the Medical Department is next reprinted, the Bureau will request the Superintendent of Documents, Government Printing Office, Washington 25, D. C., to stock copies for sales purposes to personnel desiring personal copies. Upon receipt of information from purchaser that he has a personal copy, the Bureau will place his name on the mailing list and automatically furnish without charge the changes thereto, as issued. Since the Bulletin of Bureau of Medicine and Surgery Circular Letters carries a

restricted classification, it cannot be made available for sale. Therefore, in those cases where a service individual purchases a Manual and also desires a personal copy of the Bulletin, the Bureau will provide same, and future changes thereto, without cost.

3. Procedure for return of personal copies.--The Bureau's supply of both publications is limited and it is very important that all surplus copies (except copies of the 1945 edition of the Manual of the Medical Department, which shall be disposed of locally) be returned to obviate the need for reprinting to meet future needs. Therefore, to assure that all copies will be accounted for, each ship and station having copies of subject publications aboard shall take the following action during the week of 13 August 1951:

a. Designate an individual or office to collect all personal copies from Medical Department officer personnel.

b. Retain and assign any extra office copies required.

c. Return all surplus copies to the Bureau of Medicine and Surgery, Department of the Navy, Washington 25, D. C., attention of Code 2124.

d. Advise the Bureau of the new total number of all office copies. The Bureau's mailing lists will then be revised accordingly.

Medical Department officer personnel on leave or in a transit status during the week of 13 August 1951 shall be responsible for seeing that their personal copies are returned to the Bureau.

4. With this change in policy, it is the Bureau's intention that sufficient office copies be retained as required for efficient operation. However, the number of office copies retained or requested will be subject to review by the Bureau.

C. J. Brown
Acting

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Erratum. In the United States Navy Medical News Letter, Vol. 18, No. 1, page 36, under BuMed Circular Letter 51-94, it is incorrectly stated under paragraph 1 (a), second line, "Record, NavMed-84, within 60 days..." The symbol "NavMed-84" is an error which should read "NavMed-H-4."

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